Cellulare:
transforming healthcare

Future Lanthan Hospital Model

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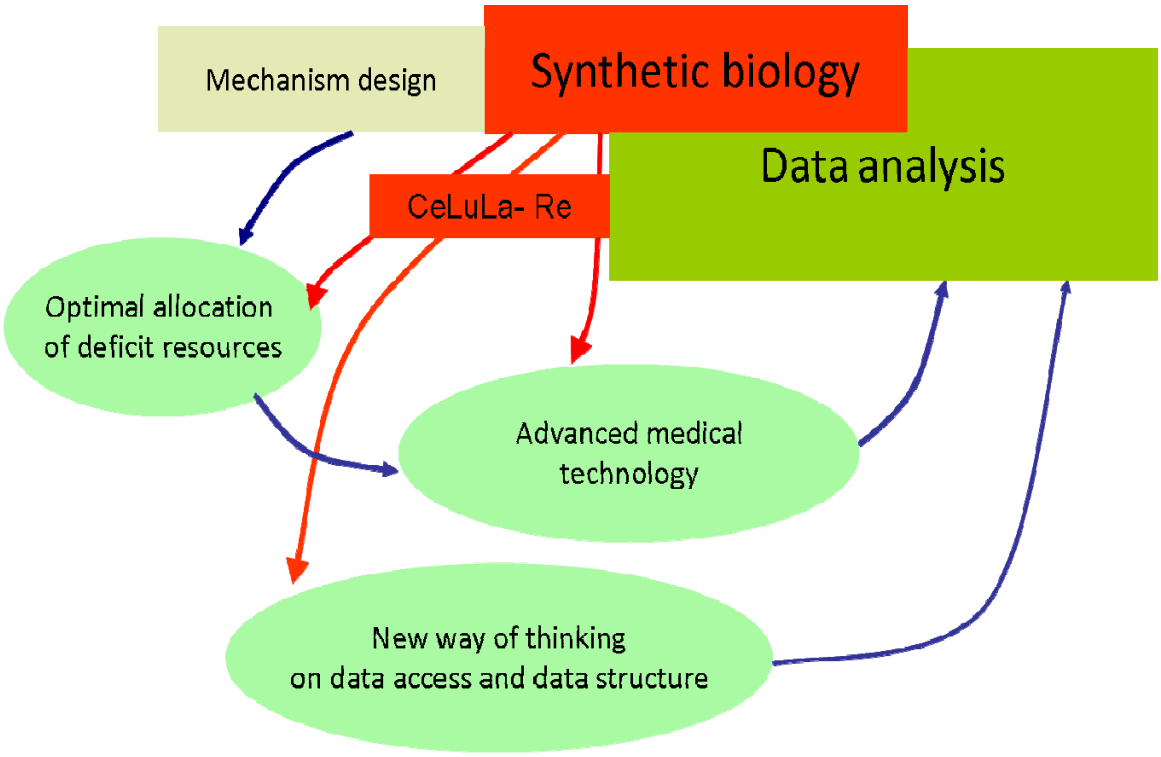
Layout



Summary

1. Background – from systems biology through synthetic biology to big data in medicine
2. New application of synthetic biology: transforming healthcare
3. New application of iGEM registry: challenging healthcare for data analysis
4. Solving optimal resource allocation problem with support of synthetic biology, economy and medicine. Step forward to open health
5. Cellulare: transforming healthcare for optimal allocation of deficit resources
6. Future Lanthan Hospital - implementation strategy through 'Cellulare'
7. Cellulare Recommendations
8. Nobel Lanthan Economy with Nobel Human Practice
9. Stable matching and mechanism design through Cellulare to Polish healthcare market
10. Closing remarks

Annex 1. Anti selfie mechanism design for smartphone MDs through Cellulare

Annex 2. KPD - optimal allocation of deficit resources need access to databases

Annex 3. Cellulare – future leaders start here

Annex 4. Creative education - workshops.

Summary

Nowadays, in the big data era, medicine will be inevitably transformed by systems biology. Rapid developments in deep sequencing, metabolomics and so called "personal medicine" have already changed medical sciences. Hence, we would like to add a valuable contribution to that healthcare transition by proposing a more synthetic biology-oriented approach for medicine. Our project ‘Cellulare’ touches both healthcare transformation for data analysis and optimal allocation of deficit resources. Our question is how to design a hospital only having access to limited resources, equip it in modern technologies (biomedical and IT), and finally how to combine modern technology and pro-ecological design in order to improve the work of healthcare. To address this difficult issue, we developed Future Lanthan Hospital Model, which is aimed to show that recovery of lanthanides (rare earth elements) from electronic waste (smartphones, tablets etc.) by synthetic biology methods, could be a beneficial supporting strategy for a modern hospital. We have proposed integration of a hospital with a supplementary synthetic biology lab, in which lanthanide remediation project could take place. First, such a solution would contribute to the public image of the hospital as a rationally functioning institution with eco-friendly profile. Secondly, it could allow to equip the hospital in modern technologies based on rare-earth metals. Simultaneously, we suggest mechanism design (engineering part of the economy) and the stable matching algorithm allowing better resource-management that would address the needs of the patients. By Future Lanthan Hospital Model we would like to show beneficial changes for society resulted from implementation of modern technologies in medicine and educate people about applications, safety and some security problems related to cutting-edge technologies. In the end we also aim to provide a contribution to the processing of medical data and open source science, since in the era of big data in medicine such measures seems to be necessary for the rapid transformation of the healthcare.

Background – from systems biology through synthetic biology to big data in medicine

A fast and efficient data analysis is expected to transform healthcare globally. Appropriate use of medical data allow us to understand medical history records: signs and symptoms, results of diagnostic and therapeutic procedures as well as digital data from diagnostic devices. However, those are traditional medical data and in the genomic era, access to data from high throughput experiments became something common. As medicine has been transformed by science and technology, we generate much more data than ever before. Furthermore, rapid progress in new technologies enable lowering the costs of healthcare by invention of telemedicine and other branches of medicine based on mobile devices.

The most current challenge in medicine is to process efficiently large amount of data and use them to make rational decisions. It is believed that data analysis is able to provide valuable information and simpler, more direct solutions to medicine-related problems. Unfortunately, there is a surplus of medical data but little knowledge how to use them in an effective way. If we want to advance healthcare with both biomedical technology and engineering itself, generated data need to be analyzed more efficiently. Efficient management of information in the healthcare and optimal allocation of deficit resources also needs data analysis.

As it was mentioned before, due to big data, medicine has started transition to be more system biology and IT-oriented. By convergence of systems biology, the digital revolution and consumer-driven healthcare vision of P4 (predictive, preventive, personalized and participatory), a new "system medicine" emerged. Thus, we are striving to add a next dimension to P4 medicine by proposing a P5 medicine (P4 + programming), which would stipulate synthetic biology approach to medicine.

Although systems biology is about understanding the complex systems, synthetic biology is about applying that knowledge to design and create artificial biological systems. We would

like to change healthcare transformation not only by application of mobile devices, but also invention of programmed biological devices. What is more we have noticed that iGEM data base is a great example of how data are properly structured and used to achieve the important scientific goal – providing the easy-to-use platform to design bigger optimized systems from standardized parts. We would like to recommend this approach as a viable solution for healthcare, making big data more useful for functional analysis and solving complicated problems in medicine.

New application of synthetic biology: transforming healthcare

P5 medicine (programming medicine)

The basic idea behind healthcare transformation to P5 medicine is to integrate synthetic biology lab with hospital (Figure 1). This is sort of start-up strategy with systems impact, which will be presented in the context of a broader healthcare transformation. The cooperation of medical professionals with synthetic biology scientists should provide an opportunity to change mental attitude to open source science and data standards in the medical community. Noteworthy, synthetic biology lab could be less expensive and may allow to rapid implementation of advancements to medical sciences. Potential assets for hospital stemmed from integration of synthetic biology laboratory performing ecological project will be discussed in the next paragraphs. Here we present only a general overview of Future Lanthan Hospital Model with 3 stages to transform healthcare by direct application of synthetic biology approach derived from iGEM competition.

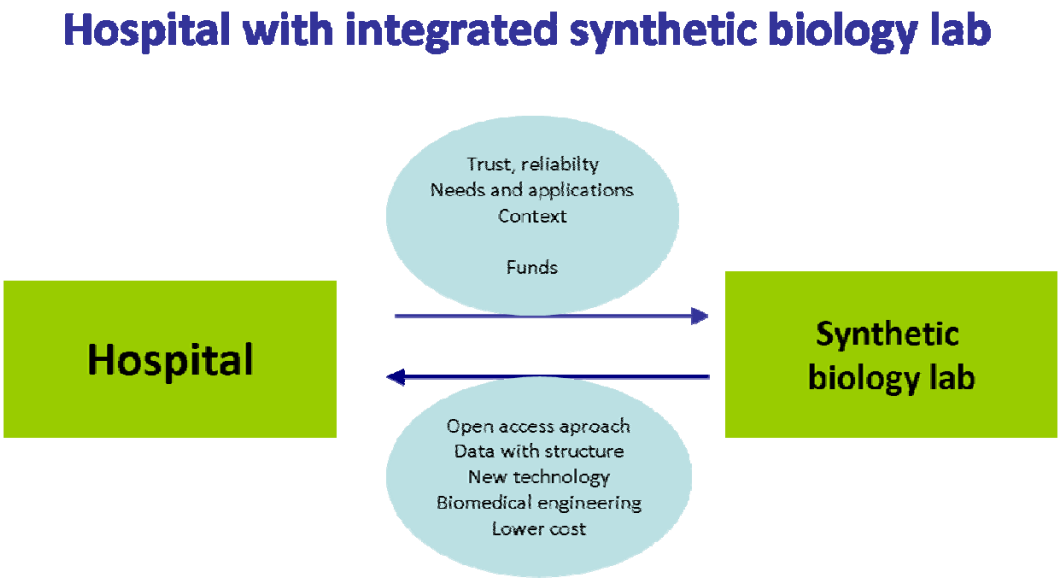


Figure 1. Transformation of the healthcare by application of synthetic biology in Future Lanthan Hospital Model – basic idea.

Transformation of healthcare:

First Stage: iGEM-based data registry and management for medical professionals

***Second Stage*:** Lanthan Recycling System For Hospitals (implementation of iGEM Warsaw Team project)

***Third stage*:** Future Lanthan Hospital Model in practice (strategy and recommendations for juridical and economical analysis as well as business model).

New application of iGEM registry: transformation of healthcare for data analysis

Medicine based on standards and sharing - IGEM for MDs (IEDM _ Internationally Engineered Data Medicine)

We would like to recommend iGEM registry as a great example of data management for medicine. The fundamental idea of medicine is to help, and philosophy of iGEM registry is to share. As help is connected with openness and sharing, both philosophies are in line. However, medicine for the sake of dealing with sensitive personal data is inherently more distant to the idea of openness. It is crucial to secure private medical records, but this fundamental requirement slows down development in medical data processing. More worryingly, there is no sufficient incentives for the strict data standardization, which is necessary to analyze them in an efficient way. Private information may be shared in only strictly regulated manner, so full openness in medicine is not possible. Nevertheless, medical data should be carefully organized to facilitate development. We believe that carefully done data analysis may allow to share only functional knowledge without compromising personal data. Nowadays, medicine becomes an information science, thus it needs to be 'programmed'. It means that a format similar to programming language is necessary to make data useful for further analysis. This is the reason why we would like to challenge medical community, showing iGEM registry as an example, and in turn initiate cooperation between synthetic biology scientists and medical professionals.

Therefore, to support open health we would like to propose a sort of IGEM competition *for MDs - IEDM _ Internationally Engineered Data Medicine* to award outstanding MDs for their endeavors to use open science approach and keeping educational open registry (Tabele 1). For instance, they could be given some grading points in their specialization course or PhD studies for attending IEDM. This could be a new way to show MD professionals the importance of keeping records in a concise and well-described format as well as facilitate their cooperation with science and IT. In case of having not enough time for patients in MDs daily routine, they need additional incentives to keep medical records structured and clear.

We suggest also, that in the next stage of this science competition, MDs should strive to develop procedures simplifying having feedback from patients. Such a strategy will lead to constant evaluation of procedures and ensuring their high quality. It needs to be emphasized that the major goal of that competition is only to improve medical sciences (especially the medical education), excluding any type of interference in treatment protocols. Such security measures should convince both medical professionals and society that openness and collaboration are not in a collision course with protection of personal data. To conclude, we can say that in our view, that open 'synthetic' approach is the best way to enrich in future medicine with new exciting ideas.

Table 1. Comparison between iGEM registry vs. IEDMs Registry (iGEM Competition for M.Ds). IEDMs main goal is to promote creative medical education and open heath.

iGEM Registry	Educational Open Registry for MDs
Documentation & Characterization: 'parts and devices are user-tested and characterized.	**New way for documentation and characterization of medical procedures:** Algorithms of treatment are described in standard format resembling programming language. Diagnostic and therapeutic procedure not strictly defined by recommendation, but based on individual MD 's experience are characterized and described in standard format.
BioBrick standard: usage of standard format. **'**Assembling two or more basic parts results in a new, composite part.'	**MedicBrick format** usage of standard format based on algorithmical principles inspired by programming languages and BioBrick standards.

The Catalog of Parts and Devices: ‘many ways to find parts: the catalog has been improved to allow to browse collection by part type, chassis, function or by several other ways.’ We made categories much more important in terms of classifying parts to form the basis of the catalog system	**Functional catalog:** many ways to find diagnostic and therapeutic procedures by functional linkage. Classification focused on health not on arbitrary defined disease.
Open Medical Community: ‘Wiki tools allow user to edit entries, see recent changes, etc. Part tools can be used to edit the database information about a given part’. ‘As part of the synthetic biology community's effort to make biology easier to engineer.’	**Open Medical Community:** Wiki based tools with access only for MDs. Open source editing in medical professionals’ communities. The goal is to make medicine information science more accessible to program procedures.

Solving optimal resource allocation problem with engineering part of biology, economy and medicine. Step forward to open health.

In previous section we presented the bottom-up strategy to make medical community and society more open for data analysis and open source movement. In the next stage of healthcare transformation, it is crucial to set perspective for rational design of healthcare institutions. We would like to suggests some concepts for integration of novel tools allowing to solve optimal allocation problems in healthcare market and to equip institution with modern devices. Proposed tools are derived from engineering part o biology, medicine and economy.

Tools:

Synthetic biology is the basic tool in our comprehensive strategy. The ultimate goal of this discipline is to design new organisms with more optimized genome. The aim is to provide efficient tools to engineer into biological devices which may find direct and indirect applications in medicine, allowing to lower the costs of medical procedures and technologies. Cooperation between synthetic laboratory and hospital may facilitate the implementation of these changes. In our strategy we consider synthetic biology also in the categories of tools aimed at supporting open source science movement in medicine.

Medical technology (medicine)

Medical technology provides versatile tools which may be used to lower the cost of healthcare management and provide more accessible care for everyone. Telemedicine allows MDs to focus on most urgent cases on site, remaining education of patients, extended rehabilitation and some simple diagnostic for teleservices. Some typical medical devices (robots, lasers) are expected to work in more efficient way. Importantly, some smartphone-based medical technologies may lower overall costs and ensure easier access to diagnostics. Effective electronic managing system will be ensured only if devices are well integrated in the hospital.

Mechanism design (economy)

The aim is to show comprehensive strategy for making modern healthcare more accessible. We would like to imply that mechanism design is the optimal way to achieve our goal – to provide a comprehensive strategy to create more accessible healthcare. To give general insight what mechanism design really is, one can cite Eric Maskin who has laid foundations for mechanism design theory:

"The theory of mechanism design can be thought of as en engineering part of economy. Much of theoretical work focus on existing institutions. The theorists want to explain or forecast economic or social outcome that this institution generate. Mechanism design reverse the direction it begins by identifying desired outcomes (goals) and continues with asking if

institution can be designed to achieve in order to achieve those goals?" said Erick Maskin (Nobel Prize Winner) [1]

Mechanism design (reverse game theory) is a field of economy that focus on creating new incentives and rules for economics aimed at realization of utilitarian social goals rather than personal pursuits. Hence, it may transform healthcare allowing to better design markets as well as redesign of institution itself, which ensures more efficient way of allocation of deficit resources. Mechanism design theory focuses on analyzing the way in which institutions efficiently allocate public goods and services. It optimizes systems by reducing selfish behavior of some individuals. Since we aim for efficient allocation of the resource, mechanism design seems to be a good support for rational decision making in incomplete information state. It may identify efficient trading mechanisms, regulation schemes and voting procedures on healthcare market.

Cellulare: transforming healthcare for optimal allocation of deficit resources

We recognized both biological and mobile devices as tools to providing advanced technology to healthcare in a cost-reduced manner. As 'Cellulare' is focused on lanthanides bioremediation, we want to propose strategy to optimal allocation of these elements and other deficit resources on healthcare market. 'Cellulare' could be treated as an example how to implement a comprehensive strategy to achieve these goals by means of synthetic biology, medical technology and mechanism design tools merged together (Figure 2). Later, this strategy would be applied by hospitals via Lanthan Recycling System.

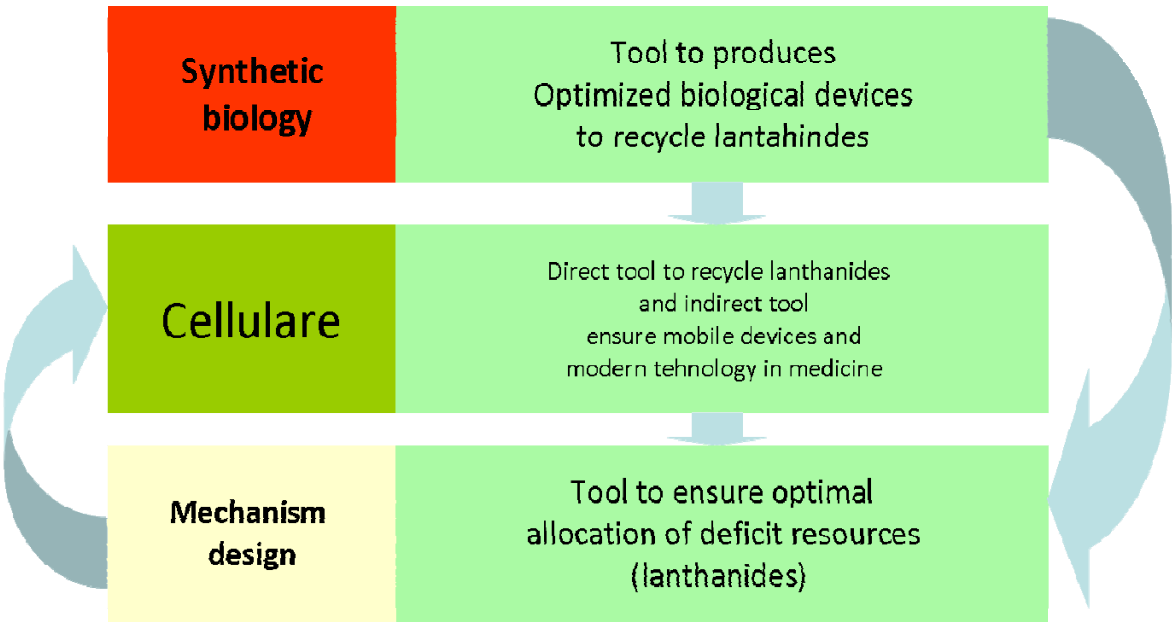


Figure 2. Cellulare: transforming healthcare for optimal allocation of deficit resources

Lanthan Recycling System for Hospitals

The very idea of Lanthan Recycling System for hospital derives from the fact that lanthanides are nowadays deficit resources with broad application including medical industry (Figure 4). 'Cellulare' has been aimed at design a bacterial system capable of detecting and binding lanthanides in order to extract these ions from electrowaste, thereby recycling these valuable metals more effectively. In other words, the long term goal was to introduce an eco-friendly retrieval technology for metal extraction. Then we envisaged that our system can be applied also in healthcare, since it extensively use lanthanides in technologically advances devices and therapies.

Future Lanthan Hospital - implementation strategy through 'Cellulare'

As it was mentioned before, on the basis of Lanthan recycling system we created model of Future Lanthan Hospital - healthcare institution fully supplied with modern technologies based on rare-earth metals (lasers, surgical robots, MRI, etc.) as well as with mobile and telemedicine technologies (Figure 3. A). Furthermore, we tried to define specific target groups of interests for this model. As much as we are concerned, those groups are wards and healthcare centers workers, which require lanthanide-based technologies (Figure 3.B). Thus, they could benefit mostly from practical implementations of our recycling system.

Specific target group 1 : oncology professionals

Modern oncology center - transforming oncology with Cellulare

MRi and Molecular Imaging including molecular MRI (advanced visualization in oncology)

Surgery Robots and Medical Lasers (surgical oncology)

Novel terapies in oncolgy (photodynamic therapy)

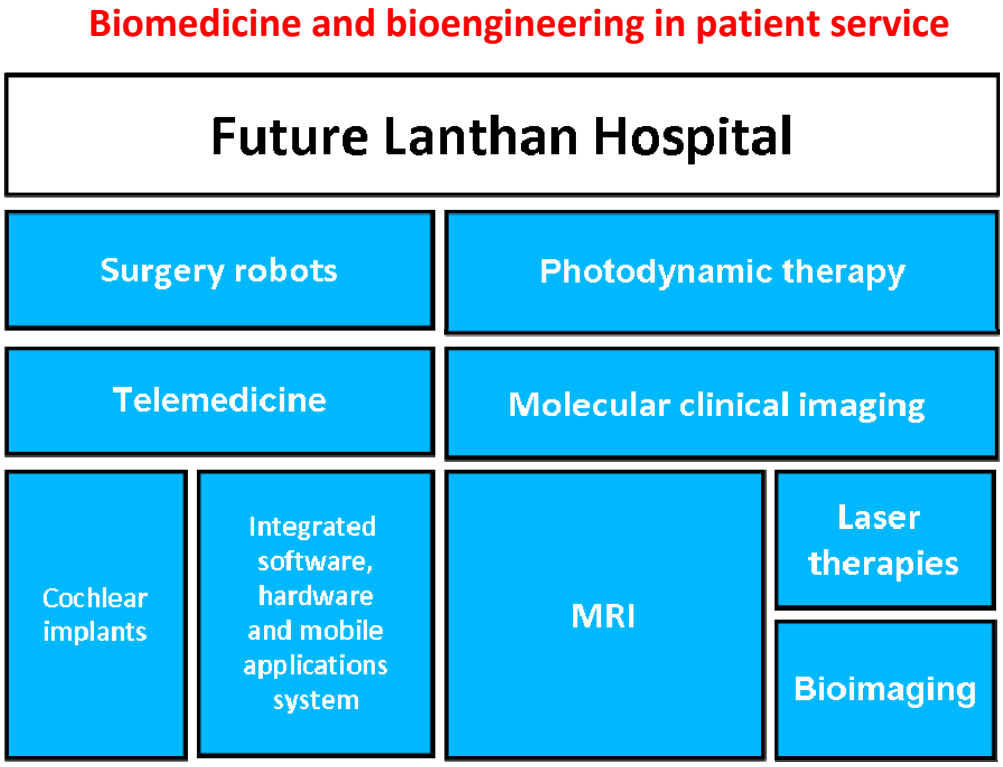
Telemedicine, Smartphones and tablets for medical doctors (large amount of data - genetic disease and long-term systemic treatment)

Specific target gropup 2 : Audiophonology professionals

Modern hearing center - transforming audiophonology with Cellulare

cochlear implants, MRI, bioimaging, teleaudiology

A.



B.

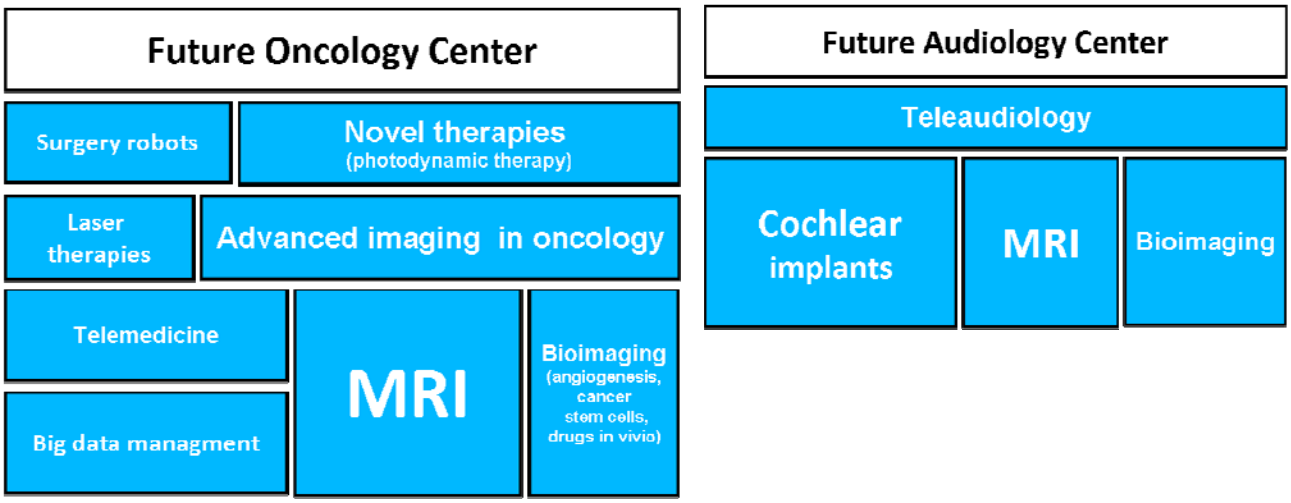


Figure 3. Future Lantan Hospital – idea of lanthan- based technology which pieces can be perceived as Lanthanbrick for Lanthan hospital. A. "Building" future hospital with modern biomedical technology and IT solutions from "LanthanBricks". B. "Building" future wards and future medical centers on the basis of Lanthan- based technology

Cellulare Recommendations:

Firstly, we recommend to use interdisciplinary tools designed using biological, medical and economical principles in integrated, complex manner.

Specific Cellulare Concept: If we intended to supply a hospital with medical devices and our funds are limited, we should forecast what hospital could possibly exchange with medical companies to get their products. Such idea may be consider as a kind of barter trade. As most of our desired products contain lanthanides (which are deficit resources on global market), becoming a provider of lanthanides appears to be an excellent solution for hospitals. However, currently available extraction methods are rather cumbersome and expensive, thus a cooperation with synthetic biology lab could ensure cheaper method of their recycling from electrowaste. If new industrial methods are developed (with hospital support), such strategy could benefit in financial gains and access to modern technologies. Nevertheless, it requires development of a proper business model. We suggest that hospital should introduce appropriate law regulation based on mechanism design theory not only to prevent selfish behavior in the decision making process, but also to achieve optimal allocation of following resources: funds, recycled lanthanides and gained medical equipment.

Secondly, we would like to propose a strategy allowing the healthcare industry and helth-tech startups to work together.

Specific Cellulare Concept: We believe that there is one lacking element crucial for cooperation between technological companies and hospitals with integrated synthetic biology lab. Namely, a presence of startup companies allowing to a barter exchange process of lanthanides and medical devices. Such a hypothetical company should also insist on collaboration with industry to initiate lanthanide recycling on the large scale. This allow to exchange recovered lanthanides with tech-oriented companies. Afterwards, these companies should equip the hospital with modern technologies based on lanthanides.

Third, we would like to propose transfer of modern economic concepts to healthcare market promoting startups focused on resolving optimal allocation problem.

Specific Cellulare Concept: As lanthanides are deficit resources, they required proper allocation on healthcare market and, by similarity, lanthanide-based technologies needs proper allocation inside hospital. Lanthanides have broad application in many medical devices and technologies, which are provided by different companies. Therefore an efficient kind of auction should be designed in order to exchange lanthanides. According to previous paragraphs, we recommend implementation of mechanism design theory in negotiations between companies to ensure the most efficient way of bargaining and achieving more social-oriented goals - making technologies more accessible for patients. In next stage it is necessary to think about optimal allocation of medical devices in the hospital - preferences of different wards must be taken into consideration. In this case stable matching algorithm should be applied. Suggested method is expected to provide much people with resources they really need. Thus, in case of implementation of Future Lanthan Hospital model, we propose a solution inspired by the Nobel Prize in Economy, which we termed "Nobel Lanthan Economy".

Nobel Lanthan Economy with Nobel Human Practice

→ Eric Maskin (Nobel Prize in Economics 2007): mechanism design

Maskin is a Nobel Prize winner, who has contributed to foundation of mechanism design theory. What is more, together with James Bessen [2], he argued 'innovation is "sequential" (so that each successive invention is built on the success of its predecessors) and "complementary" (so that each potential innovator takes a complementary research strategy)'. Their sequential model of innovation is supported by evidence from a software industry, in which imitators can provide benefit to both the original inventor and the whole society.

New Application: mechanism design through iGEM for healthcare market

iGEM philosophy bears a resemblance to Maskin's view on achieving social goals, and it is based on competition-driven strategy leading to better results. In the first step of Future Lanthan Hospital Model we would like to develop IEDMs to change the attitude of medical communities to open source philosophy. It is beneficial to use Maskin's theory to accomplish some social goals, such as developing an iGEM Human Practise for hospital.

Cellulare Application: providing a proper solutions and law regulations in negotiations between healthcare startup and giant tech companies

We aim to develop a startup-like model of healthcare institution which additionally has a system impact on the industry. As we mentioned before, the mechanism theory should reduce selfish behavior of both parties involved in business negotiation. According to works of Brahm and Mittis [3], a proper use of mechanism design principles is able to impose honest bargaining. The following excerpt from their seminal paper [3] shows the basic idea:

"A classic challenge in contract and property law is unstructured negotiation between two parties with asymmetric information (i.e. each party has different private information) under bilateral monopoly (each party must negotiate with other to try to reach an agreement), which often leads to prohibitively high transaction costs, and if the parties fail to agree, social costs as well. In this situations law should incorporate principles of mechanism design, a methodology which employs structured procedures to give the parties incentives to reach agreement. In terms of contract theory, mechanisms constitutes algorithmic altering rules that reduce, if not eliminate, inefficient transactions." [Law and mechanism design: procedures to induce honest bargaining]

The enormous challenge and long term goal for the Future Lanthan Hospital Model is to provide a valuable contribution in the introduction of law regulation based on mechanism design.

→ **Alvin Roth** (Nobel Prize 2012 in Economics): stable matching algorithm for healthcare - mechanism design without money

Alvin Roth demonstrated that stability is the key to understanding the success of particular markets, including healthcare market. He has adjusted stable matching algorithm to real practical problems. In this context, stable matching refers to finding an optimal superposition of two sets of elements, given a set of preferences for each element. Stable match in which there is no incentives to "change" any matching, is to achieve by usage of top trading cycles algorithm. It's principle is very simply and is based on an initial allocation of objects and subsequent swapping [4]. Roth adapted that theory to real problems in healthcare. His examples include the assignment of new doctors to hospitals and human organs for transplantation. The last one is called Kidney Paired Donation (KPD) [4]. So in fact, Roth received Nobel Prize for showing the best way to match people with what they really need. As his contribution refers to kidney transplantation, he is perceived as an economist whose work actually saves people lives. Even Roth said *"Well, you know, market design is a helping profession, we help our surgical colleagues to save some people's lives."*. We are aimed at using his theory in business model for startup company, but in first stage of transformation we are about to test it in Human Practice for Future Lanthan Hospital. To conclude, our dream is to match patients with things they really need.

New application: developing business model for startup company which exchange goods or conduct auctions

Roth findings provided ground for further analytical developments as well as practical design of institutions. One of the main feature of these improvements refers to situation when prices are not a part of matching process. From the ethical point of view, prices itself should not be used to allocate deficit resources. However, algorithms which include prices work in similar manner and they may produce stable matches. In fact, price matching is closely related to auctions,

where objects are matched with buyers, hence prices are decisive [4]. Researchers who relate matching algorithms to auction, recently published interesting theoretical results, which appear to be applicable in practice [4]. Interestingly, some companies have already gained some profits from application of aforementioned algorithms in practice [4]. As Makin's mechanism design is directly connected with the auction problem, we would like to point out some connections between this two theories. According to our believe it is beneficial to integrate these theories in business development for startup companies which exchange goods or conduct auctions.

Cellulare application: ensuring proper wards and centers in healthcare institutions with what patients really need

We would like to propose to use Roth's findings in developing our Future Lanthan Hospital model. It can be noticed that exchanging lanthanides for medical devices is similar to barter trade in kidney paired donation problem or during some auctions (depending whether chosen business models presumes using prize), so adaptable matching algorithm could be useful. What is more, when medical devices are gained for hospital, we will want to allocate them in possibly optimal way (including preferences of particular wards, centers and MDs determined by the patients needs).

Stable matching and mechanism design through Cellulare to Polish healthcare market

Since we are focused on our long term goals - implementation of Future Lanthan Hospital Model, we would like to promote transfer of mentioned economic concepts to Polish healthcare market, by connecting our project 'Cellulare' with promotion of beneficial economic concepts in Poland. We would like to promote mechanism design via 'anti selfie mechanism design for smartphone MDs by 'Cellulare' action connected with Future Lanthan Hospital Model (see annex 1). It will allow us to promote a notion of combining modern technology with rational and eco-friendly profile of institution as well as rational allocation of resources. The second economic conception - stable matching algorithm, will be supported and promoted by

project on implementation of KPD in Poland (see annex 2). That actions should help with changing the attitude of society, especially medical community's to the idea of sharing and openness. By KPD project, we want to emphasize direct economical gains from changing the attitude. Simultaneously, we would like to point out that optimal allocation of resources needs more open access to data. During development of KPD project, we fully realized problems concerning data structure and limited access to them as well as openness of medical professionals.

Closing remarks

To sum up we would like to encourage to seek new possibilities of collaboration of the interdisciplinary projects through new ways of communication in science. First we are going to improve our project to make it suitable for further collaboration. This is to achieve by support of Scientia Crastina (latin for 'The Science of Tomorrow') which is a networking platform for the discussion of scientific communication and science communication. This way we can make our ideas clear for people of different background (economics, law). We have started so far collaboration with members of Collegium Invisibile and the program 'Leaders of healthcare market' supported by Foundation 2065 im. Lesław A. Pagi (see anex 3) so we need to prepare our language in the way facilitating further actions and performing some analysis to develop business model for Lanthan Hospital. That is why we have proposed a solution to facilitate the data acquisition, simultaneously changing the social attitude towards transformation of the healthcare. We would like to use that data to perform several analysis connected to Future Lanthan Hospital.

Finally we would like to put emphasis on creative medical education with interdisciplinary approach to find future MDs on the border of sciences iGEM Team members have preapared workshops for highly gifted students interested in biology and medicine (see anex 4) We wanted to spread the idea of Future Lantan Hospital and potential applications of lantahnides in medicine, as we thinking of our long term gols from the beginning - we want our project Cellulare to have real aplication and meet people needs and contribute to tranforming

healthcare through synthetic biology approach. We need to adress future leaders and prepare them for oolbaoration in iterdisciplinary projects on the bounderies of science, business and technology. We need new way of communication is science to make big dreams real.

Acknowledgments

We would like to thank Piotr Dworczak for inspiration of mechanism design theory and crucial contribution to project on estimation of potential gains from impementation of KPD pilot program in Poland. What is more, we would like to acknowledge Piotr Byrski for cooperation in worshops on Future Hospital and Piotr Migdał for providing us with the cover photo.

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